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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,943	12/29/2004	Martijn Gipmans	12810-00140-US	5073

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EXAMINER	
BAGGOT, BRENDAN O	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 12/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/519,943	GIPMANS ET AL.	
	Examiner	Art Unit	
	Brendan O. Baggot	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7 is/are rejected.

7)☒ Claim(s) 8-11 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 29 December 2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Restriction / Election

1. The Office acknowledges the receipt of Applicant's Application, filed 12/29/04. Claim 1-11 are pending in the instant application. Claims 8-11 are either improper multiple dependent claims or depend upon same, as stated below.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Sequence Listing

2. Applicant's computer readable format sequence listing has been entered.

Specification

3. Applicant is required to update the status (pending, allowed, etc.) of all parent priority applications in the first line of the specification. The status of all citations of US filed applications in the specification should also be updated where appropriate.

Claim Objections

4. Claims 8-11 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim (e.g. "any of. . .") must recite the alternative only. Claims 8-9 and 11 should be amended to

recite "---any one of---" Claim 11 depends from another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112, 1st, paragraph, written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2-4, 6-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' claims are broadly drawn to transforming any plant with any sequence from any species of any length having as little as 60% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 2, or variants thereof, having non-exemplified and unspecified activity, any vector, cassette, plant organism, tissue, organ part, cell, or propagation material containing said sequence, any plant transformed therewith, any seeds comprising any sequence having as little as 60% sequence identity to SEQ ID NO: 1. The claims also encompass SEQ ID NO: 1 and SEQ ID NO: 2 homologs from other species. The claims also encompass SEQ ID NO: 2 homologs from other species. The implication is that there is a gene and a protein other than that disclosed which exists in nature, but the structure thereof is not known.

Applicants describe SEQ ID NO: 1 and SEQ ID NO: 2. (See the sequence listing).

Applicants do not describe sequences which are merely 60% identical to SEQ ID NO: 1 or SEQ ID NO: 2, variants of SEQ ID NO: 1 or SEQ ID NO: 2, the crystal structure of SEQ ID NO: 2, or the allosteric or active sites of SEQ ID NO: 2. Applicants fail to even teach the reaction catalyzed by the enzyme with the sequence of SEQ ID NO: 2.

Applicants fail to describe a representative number of variants of SEQ ID NO: 2 or other sequences. Applicants only describe SEQ ID NO: 2. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of SEQ ID NO: 2. Applicant's don't even describe the reaction catalyzed by SEQ ID NO: 2 let alone the common structural features the genus of variants of SEQ ID NO: 2 or 60% identical to SEQ ID NO: 2 or even a representative number of species. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*.

Furthermore, given the lack of description of the necessary elements essential for variants of SEQ ID NO: 2 or 60% identical to SEQ ID NO: 2, it remains unclear what features identify said genus of variants of SEQ ID NO: 2 or 60% identical to SEQ ID NO: 2. Since the genus of variants of SEQ ID NO: 2 or 60% identical to SEQ ID NO: 2 has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Moreover, sequences that are 60% complementary to SEQ ID NO: 2 encompass naturally occurring allelic variants, mutants of SEQ ID NO: 2, as well as sequences encoding proteins having no known oil profile modifying activity, of which Applicant is

not in possession. Accordingly, the specification fails to provide an adequate written description to support the genus of sequences 60% sequence identical to SEQ ID NO: 2 as encompassed by the percent identity language as set forth in the claims. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

The Federal Circuit has clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Finally, the court held:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. Id.

See also MPEP Section 2163, page 174 of Chapter 2100 of the August 2005 version, column 1, bottom paragraph, where it is taught that

> [T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. *See* The Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.

Claim Rejections - 35 U.S.C. §112, first paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2-4, 6-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 1 and SEQ ID NO: 2 and yeast and *Arabidopsis* transformed therewith, yeast with increased triacylglycerol and *Arabidopsis* with increased total oil of unspecified character, does not reasonably provide enablement for sequences which are 60% sequence identical to SEQ ID NO: 1 or 2 or variants thereof or their use to alter oil in transformants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The *Wands* court set forth the enablement balancing test:

> Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). *Wands* states at page 1404, "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the 'claims.

M.P.E.P. § 2164.01(a); See also *Ex Parte Forman* 230 USPQ 546, 547 (BdPatAppInt 1986); See also *Enzo Biochem, Inc., v. Calgene, Inc.*, 188 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999).

"35 U.S.C. §112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. . . In cases involving. . .unpredictable factors. . .the scope of enablement. . .varies inversely with the degree of unpredictability. . .". *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Applicants' claims are broadly drawn to transforming plants with any sequence having as little as 60% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 2, or variants thereof, having non-exemplified and unspecified activity, any vector, cassette, plant organism, tissue, organ part, cell, or propagation material containing said sequence, any plant transformed therewith, any seeds comprising any sequence having as little as 60% sequence identity to SEQ ID NO: 1. The claims also encompass SEQ ID NO: 1 and SEQ ID NO: 2 homologs from other species. The implication is that there is a gene and a protein other than that disclosed which exists in nature, but the structure thereof is not known.

Applicants teach SEQ ID NO: 1 and SEQ ID NO: 2. (See the sequence listing).

Applicants do not teach sequences which are merely 60% identical to SEQ ID NO: 1 or SEQ ID NO: 2, variants of SEQ ID NO: 1 or SEQ ID NO: 2, the crystal structure of SEQ ID NO: 2, or the allosteric or active sites of SEQ ID NO: 2. Applicants fail to even teach the reaction catalyzed by the enzyme with the sequence of SEQ ID NO: 2.

The Nature of the Invention

The claims are drawn to methods and compositions relating to transgenic plants. The invention is in a class of inventions which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The Breadth Of The Claims

The claims are broadly drawn to and encompass transforming plants with any any sequence of any length from any species having as little as 60% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 2 having non-exemplified and unspecified activity, any vector, cassette, plant organism, tissue, organ part, cell, or propagation material containing said sequence, any plant transformed therewith, any seeds comprising any sequence having as little as 60% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 2 over unspecified portions and having exemplified and non-exemplified activity. The claims are further drawn to "variants" of SEQ ID NO: 1 and 2.

The broad language expressly includes sequences with less than 100% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 2 from any species with any sequence having any function, including sequences encoding proteins with no total oil increasing activity.

With regard to sequences having less than 100% sequence identity and sequences, the breadth of these claims encompasses unspecified base substitutions, deletions, additions, insertions, and combinations thereof without retaining function or with an

inadequate function.

Quantity Of Experimentation

The quantity of experimentation in this area is large since Applicant would have to identify homologs, clone the homologs, do enzyme assays to confirm the enzymes have activity, select the homologs with high activity, transform a sufficient number of plants to offset position effects, select out the high copy number transformants, and screen the transformants for high expressing lines. This effort is an inventive, unpredictable and difficult undertaking in itself. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

In addressing sequences having 60% sequence identity with SEQ ID NO:1 or SEQ ID NO: 2, neither Applicant's disclosure nor the state of the prior art teaches which region(s) of SEQ ID NO: 2 should be retained for total oil content increasing activity, or whether SEQ ID NO: 2 would encode a protein having total oil content increasing activity and which would tolerate deletions, additions, and/or substitutions. Applicant provided no working example of any sequences from any species having less than 100% sequence identity with SEQ ID NO:2.

Voelker et al., teaches that the quantity of experimentation for oil pathway manipulation can involve intensive research in several laboratories and yet remain elusive for some time. (Voelker, et al (2001) Plant Mol. Biol. 52, 335-361, p. 340, first full parag.).

The Unpredictability of the Art and the State of the Prior Art

Modifying plant oil content is well-known to be unpredictable.

Post-Beittenmiller, et al., (1989) Plant Cell 1:889-899) teach that alteration of lipid biosynthesis is unpredictable. Post-Beittenmiller postulated that transgenic plants overexpressing Acyl carrier protein (ACP) with a transit peptide under the control of the rubisco small subunit promoter would alter lipid biosynthesis. Post-Beittenmiller et al found that while ACP protein levels in transgenic plants were expressed at a 2-3 fold higher level than endogenous ACPs, lipid analyses of the transformed plants indicated that the increased ACP levels caused no significant alterations in leaf lipid biosynthesis. (*See* the abstract).

Stephanopoulos, et al., (1993) Tibtech 11:392-396) teaches that manipulation of enzymatic reactions that are part of a product-forming pathway has led to failed or marginally successful results in fatty acid biosynthesis despite the success of others using similar approaches. (page 393, right column, 1st paragraph). Stephanopoulos continues that inserting just any gene in a pathway, without first determining the key branch points is not a rational experimental design and that the skilled artisan should first determine the critical or principal nodes which control metabolic flux through the pathway so as to favor the desired product and to disfavor the unwanted side products. (*See* Figure 2, abstract, pages 392-396).

There is abundant prior art to suggest that identifying proteins via percent identity alone is difficult, unpredictable and unsuccessful.

It is well established that sequence similarity is not sufficient to determine functionality of a coding sequence. *See* the teachings of Doerks (TIG 14, no. 6: 248-250, June 1998), where it states that computer analysis of genome sequences is flawed, and "overpredictions are common because the highest scoring database protein does not necessarily share the same or even similar function's" (the last sentence of the first paragraph of page 2484). Doerks also teaches homologs that did not have the same catalytic activity because active site residues were not conserved (page 248, the first sentence of the last paragraph).

Applicants' failure to teach the enzymatic activity of YJR098c, when coupled with the teachings of Stephanopoulos and Post-Beittenmiller, and the lack of data beyond a mere statement of altered oil levels, supports an additional inference in the mind of the skilled artisan that even if some weak data showing alterations of oil levels was obtained, these data are likely little more than "a "plan" or "invitation" for those of skill in the art to experiment using the technology." *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 USPQ2d 1129(Fed. Cir. 1999); MPEP § 2164.06(b).

Working Examples

The specification has no working examples of sequences which are 60% identical to SEQ ID NO: 1 or 2, no working examples of any protein with demonstrated total oil content increasing activity, and no working examples of transgenic plants or seeds therefrom with demonstrated total oil content increasing activity.

The specification has no working examples of transforming plants with any

sequence having as little as 60% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 2 having non-exemplified and unspecified activity, any vector, cassette, plant organism, tissue, organ part, cell, or propagation material containing said sequence, any plant transformed therewith, any seeds comprising any sequence having as little as 60% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 2 over unspecified portions and having exemplified and non-exemplified activity.

The specification does provide working examples of YJR098c yeast knockouts with reduced triacylglycerol (*See* Example 1, page 27-28), YJR098c expressing yeast with increased triacylglycerol (*See* Example 2, page 28-30), and transgenic plants expressing YJR098c with "significantly higher total oil content in transgenic lines." (*See* Example 3, page 30-31).

Guidance in the Specification

The specification, while suggesting the use of the SEQ ID NO: 1, did not provide significant guidance on how to overcome art recognized problems in identifying homologs based on sequence identity alone. The specification provided no guidance on overcoming art-recognized problems with natural plant mechanisms which ensure homeostasis.

The specification also did not provide significant guidance on how to overcome art recognized problems in identifying homologs having 60% sequence identity, variants, mutants and alleles of SEQ ID NO: 1,2. It is well established that sequence similarity is not sufficient to determine functionality of a coding sequence. See the

teachings of Doerks (TIG 14, no. 6: 248-250, June 1998), where it states that computer analysis of genome sequences is flawed, and "overpredictions are common because the highest scoring database protein does not necessarily share the same or even similar function's" (the last sentence of the first paragraph of page 2484. Doerks also teaches homologs that did not have the same catalytic activity because active site residues were not conserved (page 248, the first sentence of the last paragraph).

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Accordingly, one skilled in the art cannot make and use sequences having at least 60% sequence identity with SEQ ID NO:1 without improperly extensive and undue experimentation. Without sufficient guidance, determination of what portions of SEQ ID NO: 2 would tolerate changes, additions, insertions, or deletions and without guidance on how to overcome the problems seen in expressing oil pathway proteins in transgenic plants, it is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. *See In re Wands*, 858 F.2d 731,8 USPQ2nd 1400 Fed. Cir, 1988)

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art, balanced only against the high level of skill in the art as discussed above, undue trial and error experimentation would be required to practice the claimed invention, and therefore the invention is not enabled throughout the broad scope of the claims.

Claim Rejections - 35 U.S.C. §112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-7, and any claims dependent thereon, are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Clam 1: " a polypeptide SEQ ID NO: 2" is unclear – is a subsequence of SEQ ID NO: 2 intended, or is the entire SEQ ID NO: 2 intended? If the latter is intended, the claim should be amended to insert - - - comprising - - - before "polypeptide" in line 1, part (a).

Claim 5: see reasoning above.

Claims 2 and 6 are in improper Markush terminology. MPEP 2173.05(h). It is suggested that applicant insert "--- or ---" before the final paragraph of each claim.

Claim 2, and any claim dependent thereon, fails to further limit claim 1, since they are broader than claim 1. Claim 1 is limited to SEQ ID NO: 2 while Claim 2 recites sequence variants.

Claim 2 and 6, reciting "is described by" are unclear and do not employ U.S. practice recognized terminology; replace said recitation with "--- comprises ---."

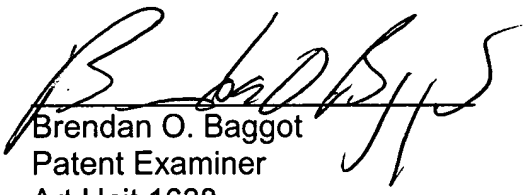
8. The Claims are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated nucleic acid at least 60% sequence identical to SEQ ID NO: 1 or encoding a polypeptide at least 60% sequence identical to SEQ ID NO: 2, or plant transformation therewith.

9. All Claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brendan O. Baggot whose telephone number is 571/272-5265. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571/272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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